

AMENDMENTS TO THE CLAIMS

1-36. (Cancelled).

37. (Currently Amended) A peptide composition suitable to discriminate between a) latent tuberculosis infection or tuberculosis under efficacious *M. tuberculosis* therapy and b) active tuberculosis or recent tuberculosis infection or re-infection wherein ~~[[i]]~~ said peptide composition ~~[[i]]~~ comprises a pool of CFP-10 peptides which consists ~~consist of a pool of~~ of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, and SEQ ID NO: 8.

38. (Previously Presented) The composition according to claim 37 further comprising two ESAT-6 peptides consisting of SEQ ID NO: 10 and SEQ ID NO: 12.

39. (Currently Amended) An *in vitro* method for diagnosing ~~[[i]]~~ different states of tuberculosis, discriminating between: a) active tuberculosis or recent tuberculosis infection or re-infection and b) latent tuberculosis infection or tuberculosis under efficacious *M. tuberculosis* therapy, whereby:

i) _____ an aliquot of whole venous blood or PBMC (peripheral blood mononuclear cells)

is admixed with an effective amount of the peptide composition according to claim 37 or 38,

ii) _____ output data on T-lymphocyte activation are collected and compared to output

values of reference samples in order to determine T-lymphocyte response,

iii) said response is scored into lack or presence of a response to the peptide composition, wherein the lack of a response correlates to: a) latent tuberculosis infection or tuberculosis under efficacious *M. tuberculosis* therapy, and the presence of a response correlates to: b) active tuberculosis or recent tuberculosis infection or re-infection.

40. (Withdrawn) An *in vitro* method according to claim 39, said method comprising the following steps:

a) admixing an aliquot of venous blood or mononuclear cells (PBMC) with the following reagents:

- Reagent 2: at least one intact protein selected in the group of ESAT-6 and CFP-10, and corresponding mixtures;
- Reagent 3: ESAT-6 pool of peptides of SEQ ID NO: 10 and SEQ ID NO: 12 diluted in a solvent;
- Reagent 4: the peptide composition of claim 37 diluted in a solvent;
- Reagent 5: the peptide composition of claim 38 diluted in a solvent; and

b) measuring T-lymphocytes response.

41. (Withdrawn) The method according to claim 40 further comprising an incubation of an aliquot of venous blood or PBMC with:

- Reagent 6: an aspecific T-Lymphocyte stimulus, as phytoemoagglutinine (PHA), positive control; and
- Reagent 7: PPD, Purified Protein Derivative.

42. (Withdrawn) The method according to claim 40 further comprising an incubation of an aliquot of venous blood or PBMC with:

- Reagent 1: CTR, complete culture medium or medium comprising the solvent concentration present in Reagents 3-5 (negative control).

43. (Withdrawn) The method according to claim 42 wherein the solvent is dimethyl sulfoxide (DMSO).

44. (Withdrawn) The method according to claim 40 whereby T-lymphocytes response is measured by: ELISPOT, FACS, or whole blood ELISA.

45. (Withdrawn) The method according to claim 44 wherein said cytokine is selected from the group consisting of: IFN-gamma, TNF-alpha, GMSF, and interleukins IL1-IL24.

46. (Withdrawn) The method according to claim 40 wherein the response is mediated by CD4 T lymphocytes .

47. (Withdrawn) The method according to claim 40 wherein, in case whole venous blood is used, said blood is placed into heparinized test tubes, and T-lymphocyte response is assessed by ELISA on plasma.

48. (Withdrawn) The method according to claim 40 wherein, in case PBMC are used, T-lymphocyte response is assessed by ELISPOT or Flow Cytometric Analysis.

49. (Withdrawn) The method according to claim 40 wherein PBMC are obtained from whole blood by density gradient centrifugation using a method based on the use of filter-equipped tubes for separation of leukocytes.

50. (Withdrawn) The method according to claim 40 wherein the incubation is carried out on PBMC from whole blood for at least 40 hours with subsequent quantitative determination of IFN-gamma production by Antigen-Specific T lymphocytes by the ELISPOT method.

51. (Withdrawn) The method according to claim 40 wherein the incubation of PBMC from whole blood is carried out for at least 16 hours with subsequent determination of IFN- γ production by Antigen-Specific T lymphocytes, said determination being both qualitative in terms of presence/absence of Antigen-Specific T lymphocytes, by FACS, and quantitative in terms of percentage and frequency of specific cells per mm³ of blood.

52. (Withdrawn) The method according to claim 40 wherein the incubation is performed on whole blood for approximately 24 hours with subsequent quantitative determination of IFN- γ production by Antigen-Specific T lymphocytes by ELISA.

53. (Withdrawn) A method to elaborate results from output values from method according to claim 40 further comprising the following steps:

- the response to Reagent 2 as defined in claim 40 is at least 3-fold higher than that to Reagent 1 as defined in claim 42 when the CTR comprises medium;
- the response to reagent 3 as defined in claim 40 is at least 2-fold higher than that to Reagent 1 as defined in claim 42 when the CTR comprises the DMSO at the same concentration present in the Reagent 3;
- the response to reagent 4 as defined claim 40 is at least 4-fold higher than that to Reagent 1 as defined in claim 42 when the CTR comprises the DMSO at the same concentration present in the Reagent 4;
- the response to reagent 5 as defined claim 40 is at least 4-fold higher than that to

Reagent 1 as defined in claim 42 when the CTR comprises the DMSO at the same concentration of the Reagent 5, and optionally, the responses to Reagents 6 and 7 as defined in claim 41 are at least 3-fold higher than that to Reagent 1 as defined in claim 42.

54. (Withdrawn) The method according to claim 53 wherein said evaluation is carried out by a computer program comprising computer program code means adapted to perform the evaluation of the response as defined in claim 53 when said program is run on a computer.

55. (Withdrawn) A diagnostic kit suitable to discriminate between: a) active tuberculosis or recent tuberculosis infection or re-infection and b) latent tuberculosis infection or tuberculosis under efficacious *M. tuberculosis* therapy for diagnosing and monitoring states of tuberculosis infection, comprising:

- Reagent 1: CTR, complete culture medium or medium comprising the solvent concentration present in Reagents 3-5, as defined in claim 40;
- Reagent 2, at least one intact protein selected in the group of ESAT-6 and CFP-10, and corresponding mixtures;
- Reagent 3: the ESAT-6 peptide pool as defined in claim 40, diluted in a solvent;
- Reagent 4: the composition according to claim 37 diluted in a solvent;
- Reagent 5: the composition according to claim 38 diluted in a solvent; and

- Laboratory materials and instructions for test procedure.

56. (Withdrawn) A kit according to claim 55 further comprising:

- Reagent 6: an aspecific T-Lymphocyte stimulus, as PHA, phytohemagglutinine;
- Reagent 7: PPD, Purified Protein Derivative.

57. (New) The method according to claim 39 wherein said output data or values are obtained by ELISPOT™, whole blood ELISA, or FACS based techniques.

58. (New) The method according to claim 39 wherein said output values of said reference samples in ii) are obtained by admixing an aliquot of whole venous blood or PBMC (peripheral blood mononuclear cells) with at least one intact protein selected from the group of ESAT-6 and/or CFP-10, or a mixture thereof.

59. (New) A diagnostic kit suitable to discriminate between: a) latent tuberculosis infection or tuberculosis under efficacious *M. tuberculosis* therapy, and b) active tuberculosis or recent tuberculosis infection or re-infection, for diagnosing and monitoring states of tuberculosis infection, comprising

a peptide composition comprising a pool of CFP-10 peptides consisting of: SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, and SEQ ID NO: 8.

60. (New) A diagnostic kit according to claim 59 wherein said peptide composition comprising a pool of CFP-10 peptides consisting of: SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, and SEQ ID NO: 8, further comprises two ESAT-6 peptides consisting of SEQ ID NO: 10 and SEQ ID NO: 12.